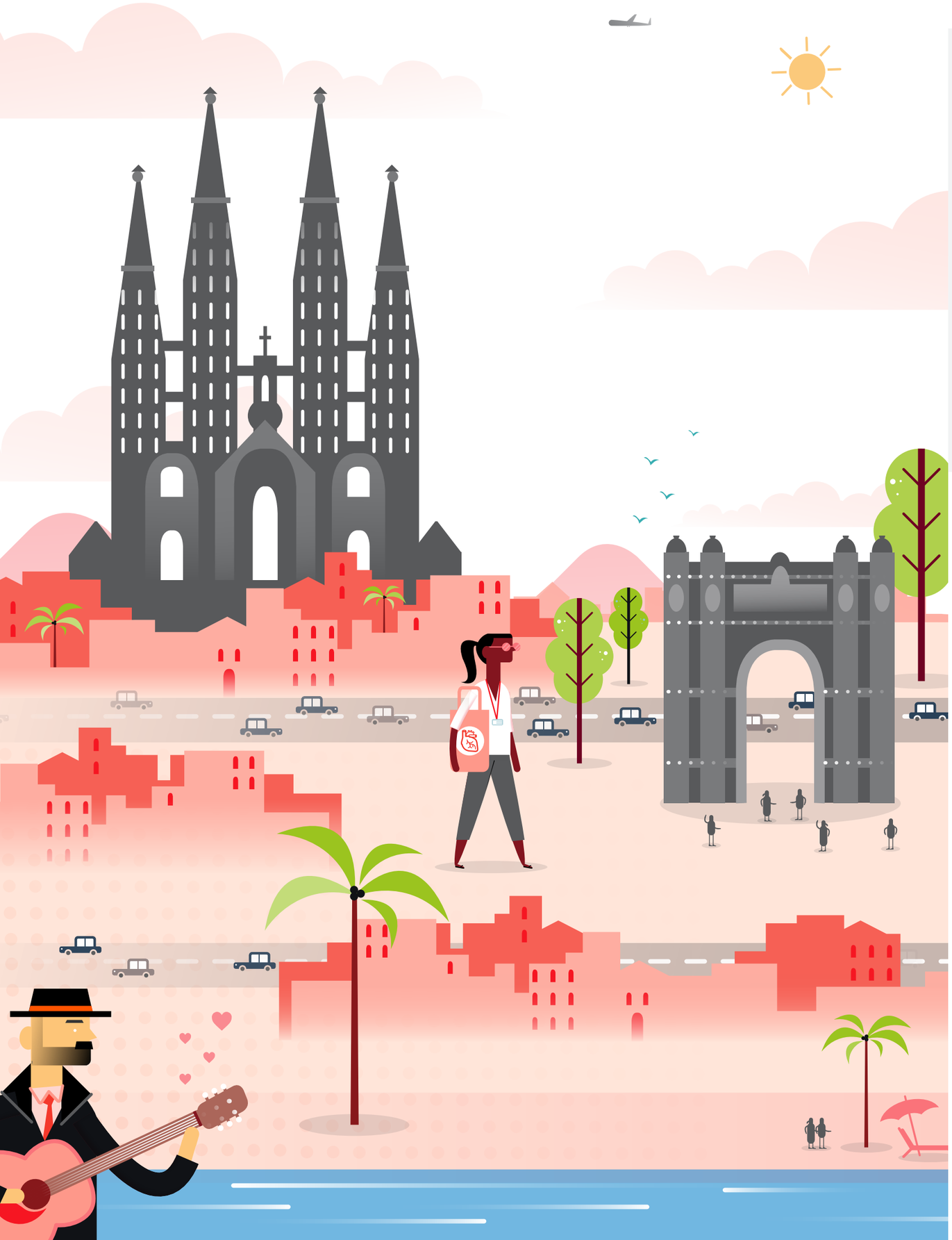

ESC ANNUAL CONGRESS 2017

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Welcome to the European Medical Journal review of the Annual Meeting of the European Society of Cardiology

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The glorious city of Barcelona, Spain was resplendent in the summer sun this August, as cardiologists from all over the world flocked to take part in the European Society of Cardiology (ESC) annual meeting. Bursting with history and culture, the Catalan capital was the ideal location for a congress that promised to carry the field of cardiology forward into the digital age. However, in order to look to the future, one must first understand the past, and this year's congress was deeply intertwined with the discipline's roots, honouring the 40th anniversary of Andreas Grüntzig's pioneering balloon angioplasty. With millions of angioplasty procedures now performed every year, this landmark event in 1977 changed the face of cardiology forever, catapulting the discipline into the future. Today, with the rapidly evolving world of technology, this year's ESC congress sought to modernise cardiology and once again bring it to the forefront of medical innovation, as Grüntzig did almost half a century ago.

The opening ceremony was an excellent introduction to the event, with its focus on education, innovation, and collaboration. Remarking on the attendance, the ESC President, Prof Jeroen Bax, said: "Nowhere else in the world can you find cardiovascular professionals from >140 countries coming together like this. This is unique. Yes, we are called the ESC, but this is a profoundly global organisation. From our very beginning, 67 years ago, we recognised that our diversity is our strength. And that philosophy has never been more important than it is today." Prof Bax then introduced Prof Eric Topol, Scripps Research Institute, San Diego, California, USA, to discuss cardiology in the digital age. Prof Topol spoke at length about modernising many of the seemingly archaic aspects of cardiology, for example, the stethoscope, which has been largely unchanged for >200 years. He spoke of the rising role of technology, from big data to neural networks and artificial intelligence, but noted the paramount importance of retaining human compassion in a digital world. The ceremony concluded by honouring the field's best and brightest for their impressive career achievements. Dr Anthony DeMaria (USA) and Prof William Wijns (Belgium) were presented with ESC gold medals for their contributions to cardiology and, in an emotional presentation, Prof Bax honoured Sir Magdi Yacoub for his lifetime of humanitarian work, saying: "Thank

you for all the good work you are doing for this world. I don't know anybody who is doing so much good work like you."

The congress was attended by >32,000 people from >140 countries, breaking the previous year's record and making it the largest cardiology event in the world. A further record was broken with regard to the number of abstracts submitted, which totalled around 11,000, of which >4,500 were selected for presentation. The meeting's programme was incredibly vast, featuring a huge range of symposia, late breaking clinical trials, keynote lectures, demonstrations, and 'Live in the Box' sessions, where clinical cases and interventional procedures were broadcast directly to the congress audience. In keeping with its theme of cardiology in the digital age, the congress also featured a corresponding mobile app, which allowed visitors to plan their itinerary in detail as well as to interact directly with speakers via a live voting system.

> "...we are called the ESC, but this is a profoundly global organisation. From our very beginning, 67 years ago, we recognised that our diversity is our strength. And that philosophy has never been more important than it is today."

With so much research on offer, it surely comes as no surprise that our following Congress Review section is packed with highlights that will be of interest to a huge range of medical professionals. We include a selection of abstract summaries, written by the presenters themselves, as well as bringing you the results from the most important clinical trials, including the revolutionary, paradigm-shifting CANTOS trial on treating inflammation in patients with cardiovascular disease.

Whether you attended this incredible meeting and wish to revisit the material, or are coming to this review with fresh eyes, we hope that it provides you with all the information needed to spark lively debate amongst colleagues and guide future research. We hope you enjoy reading and we look forward to seeing you at next year's ESC congress, held in Munich, Germany.

Congress Highlights

Long-Awaited Results of CANTOS Trial Revealed

PIVOTAL research has revealed the potential of inflammation-reducing drugs in drastically lowering the risk of both cardiovascular disease and lung cancer. Described in a ESC press release dated 27th August 2017, results of the CANTOS trial showed that lowering inflammation, independent of cholesterol, reduced cardiovascular risk, a vital finding for the 50% of heart attack patients who do not experience high cholesterol.

> "...the use of inflammation-reducing drugs was described as the beginning of a new era of preventative cardiology."

Principal investigator, Dr Paul M. Ridker, Center for Cardiovascular Disease Prevention, Brigham and Women's Hospital, Boston, Massachusetts, USA and his team focussed their attention on the human monoclonal antibody, canakinumab, which suppresses inflammation by neutralising interleukin-1β signalling. The study involved patients who had experienced a heart attack in the past and had a high degree of inflammation, indicated by elevated levels of high sensitivity C-reactive protein. The 10,061 participants were treated with aggressive standard care and were additionally randomised to subcutaneous canakinumab (50, 150, or 300 mg) or placebo treatment, once every 3 months.

Following ≤4 years of monitoring, the trial investigators observed that patients who were given 150 or 300 mg doses of canakinumab experienced a reduced risk of the primary endpoint by 15% (hazard ratio [HR]: 0.85; 95% confidence interval [CI]: 0.74–0.98; p=0.021) and 14% (HR: 0.86; 95% CI: 0.75–0.99; p=0.031), respectively, defined as the first occurrence of non-fatal myocardial infarction, non-fatal stroke, or cardiovascular death. The secondary endpoint was also the first occurrence of any of the above as well as the requirement of hospitalisation for unstable angina needing urgent revascularisation and was reduced by 17% in the 150 mg (HR: 0.83;

95% CI: 0.73–0.95; p=0.005) and 300 mg canakinumab (HR: 0.83; 95% CI: 0.72–0.94; p=0.004) groups.

After statistical analysis, the authors concluded that a significant reduction in the occurrence of primary and secondary endpoints was evident in the participants who received a 150 mg dose of canakinumab. Furthermore, exploratory analyses showed dose-dependent reductions in the rates of cancer death, particularly those due to lung cancer. Although replication of these results is required, the use of inflammation-reducing drugs was described as the beginning of a new era of preventative cardiology.

Upstream Therapies Improve Sinus Rhythm in Arterial Fibrillation Patients

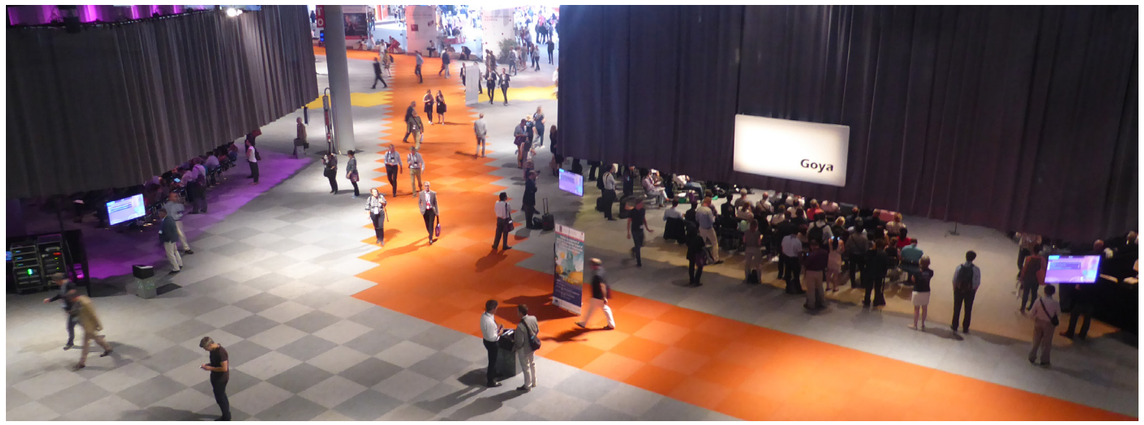
IMPLEMENTATION of four risk factor-driven upstream therapies could improve sinus rhythm in patients with atrial fibrillation (AF) and early, mild-to-moderate heart failure, according to RACE 3 trial results presented at this year's ESC congress and reported in a ESC press release dated 27th August 2017.

"AR is the most common sustained cardiac arrhythmia and affects millions of people in Europe," said principal investigator Dr Michiel Rienstra, University Medical Centre Groningen, University of Groningen, Groningen, Netherlands. Symptoms include palpitations, shortness of breath, and an impaired tolerance to exercise, and Dr Rienstra explained patients: "...have poor quality of life and are at increased risk of stroke, heart failure, or death."

Typically caused by comorbidities such as hypertension, heart failure, and obesity, AF is a progressive disease with a problematic long-term maintenance of sinus rhythm. The progression and onset of AF are caused by structural remodelling of the left atrium, and it was thought that upstream rhythm control may help prevent AF onset and progression. The RACE 3 trial was conducted to assess this hypothesis and determine whether upstream therapies were superior to conventional therapies for the maintenance of sinus rhythm.

This multicentre trial recruited 250 patients with symptomatic early persistent AF and early, mild-to-moderate heart failure. All patients received causal treatment and were subsequently split into two treatment groups, one to only receive conventional rhythm control and the other to receive rhythm control alongside four risk factor-driven upstream therapies. The upstream therapies included cardiac rehabilitation (involving physical activity, dietary restrictions, and regular counselling on drug adherence), mineralocorticoid receptor antagonists, statins, and angiotensin-converting enzyme inhibitors and/or angiotensin receptor blockers.

> "Upstream rhythm control, including meticulous treatment of risk factors and change of lifestyle, is effective, feasible, and safe in improving maintenance of sinus rhythm..."



At the 12-month follow-up, 89 of the 119 participants (75%) in the upstream therapy group presented with sinus rhythm, compared to 79 of 126 participants (63%) from the control group (p=0.021). Between the two groups, there was no difference in the number of electrical cardioversions or antiarrhythmic drug use. Dr Rienstra concluded: "Upstream rhythm control, including meticulous treatment of risk factors and change of lifestyle, is effective, feasible, and safe in improving maintenance of sinus rhythm in patients with early, short lasting AF and early, mild-to-moderate heart failure. The upstream therapies also improved treatment of cardiovascular risk factors."

Positive Results from the CASTLE-AF Trial

CATHETER ablation was found to produce improved outcomes in the treatment of left ventricular dysfunction and atrial fibrillation in the CASTLE-AF trial presented at this year's ESC congress. The results were reported in a ESC press release dated 27th August 2017 and showed that catheter ablation produced lower rates of both mortality and hospitalisation for worsening heart failure when used to treat atrial fibrillation in comparison to conventional drug treatment.

The trial in question, co-led by Prof Nassir F. Marrouche, Comprehensive Arrhythmia Research and Management (CARMA) Centre, University of Utah, Salt Lake City, Utah, USA, and Prof Johannes Brachmann, II Med. Hospital Klinikum Coburg, Coburg, Germany, enrolled 397 patients from >30 clinical centres worldwide. Patients all had symptomatic paroxysmal or persistent atrial fibrillation and heart failure with ejection fraction <35%, and each had implantable cardioverter defibrillators with Home Monitoring™ features to allow continuous observation of atrial fibrillation. The primary endpoint of the study was the composite of all-cause mortality and unplanned hospitalisation for worsening heart failure; secondary endpoints were all-cause mortality and heart failure hospitalisation.

Patients were randomised to receive radiofrequency catheter ablation or conventional drug treatment recommended by the American Heart Association (AHA) and ESC, and at a median of 37.8 months follow-up it was found that the primary endpoint was significantly lower in those receiving ablation (28.5%) compared to the control group (44.6%) (hazard ratio [HR]: 0.62; 95% confidence interval [CI]: 0.43–0.87; p=0.007). This trend continued for the secondary endpoints, with catheter ablation associated with all-cause mortality of 13.4% compared to 25.0% with conventional treatment (HR: 0.53; 95% CI: 0.32–0.86; p=0.011). Furthermore, those treated with catheter ablation had a 20.7% rate of hospitalisation due to heart failure compared with 35.9% in the conventional treatment group (HR: 0.56; 95% CI: 0.37–0.83; p=0.004).

> "This study has the potential to change the way physicians manage many patients suffering from heart failure and atrial fibrillation."

Prof Marrouche commented on the results: "We found that compared to those receiving conventional treatment, patients receiving catheter ablation were 38% less likely to experience the primary endpoint, 47% less likely to die, and 44% less likely to be hospitalised with worsening heart failure. A significant number of patients undergoing the ablation treatment were still in normal rhythm at the end of the study."

It was seen as a limitation to the study that all the patients had an implantable cardioverter defibrillator, which could have affected mortality across both groups. Regardless, Prof Marrouche was positive about the impact of the trial, and commented: "Until now, we had no evidence that ablation, arrhythmia medications, or any other treatment was superior to another in saving lives and reducing hospitalisation," adding: "This study has the potential to change the way physicians manage many patients suffering from heart failure and atrial fibrillation."

New Treatment for Patients with Peripheral Artery Disease

A REDUCTION in major adverse cardiovascular and limb events in patients with peripheral artery disease (PAD) can be achieved by adding rivaroxaban to aspirin as a therapeutic option, according to results from the COMPASS trial, as reported in a ESC press release dated 27th August 2017. Globally, PAD is believed to affect 200 million people and these individuals are at a heightened risk of heart attack, stroke, death from cardiovascular causes, and limb-threatening ischaemia. Currently the standard antithrombotic therapy used is aspirin; however, this is only moderately effective.

> "This is an important advance for patients with peripheral artery disease."

Researchers in the COMPASS trial investigated two potential therapeutic options for protection against major adverse cardiovascular and limb events in 7,470 patients with PAD of the lower extremities and carotid artery disease recruited from 33 countries (e.g. severe limb ischaemia and amputation): rivaroxaban and rivaroxaban plus aspirin. Patients in the rivaroxaban group received two daily doses of 5 mg rivaroxaban, patients in the rivaroxaban plus aspirin group were given 2.5 mg rivaroxaban twice daily and 100 mg aspirin once daily, while the aspirin group received the standard aspirin therapy of 100 mg once per day. The trial's primary endpoint was a combination of stroke, myocardial infarction, or cardiovascular death.

It was found that patients in the rivaroxaban arm had reduced major adverse limb events when compared to those in the standard aspirin therapy arm but no reduction in major adverse cardiovascular events. When cardiovascular and limb events were taken together, rivaroxaban alone was not more efficacious than aspirin. However, in the rivaroxaban plus aspirin arm, there was a 31% reduction in major adverse cardiovascular or limb events compared to the aspirin arm. This translated to a 46% reduction in limb threatening ischaemia (including amputation) and a 28% reduction in the risk of cardiovascular death, stroke, or heart attack.

Speaking about the impact of these findings, the leader of the PAD component of the COMPASS trial, Prof Sonia Anand, Department of Medicine, McMaster University, Hamilton, Canada, declared: "This is an important advance for patients with peripheral artery disease." She went on to explain: "To now have a therapy that reduces major adverse cardiovascular events and major adverse limb events by one-third is going to be a great benefit for these high-risk patients."

Blood Pressure Lowering Efficacy of Renal Denervation

BLOOD PRESSURE of uncontrolled hypertensive patients is significantly lowered following treatment with a renal denervation procedure, according to a ESC press release dated 28th August 2017. By applying the lessons learnt from the SYMPLICITY HTN-3 trial, scientists designed the SPYRAL HTN-OFF MED study to test the safety and blood pressure lowering efficacy of the multi-electrode Symplicity Spyral renal denervation system (Medtronic, Minneapolis, Minnesota, USA).

Patients were selected based on having uncontrolled hypertension, defined as a systolic blood pressure measuring 150–180 mmHg and a diastolic blood pressure >90 mmHg, as well as a 24-hour mean systolic blood pressure of 140–170 mmHg. Blood pressure was noted at baseline and participants were assigned to either a revised procedure for renal denervation treatment involving the main renal arteries and branches, or a sham procedure.

> This is particularly important as even small reductions correlate to significant reductions in death, stroke, and overall cardiovascular risk.

The 3-month results, presented at this year's ESC congress, described the blood pressure measurements after treatment of the first 80 patients, including 38 who received renal denervation and 42 from the sham procedure group. There was no significant reduction in the systolic and diastolic blood pressure in participants from the sham procedure arm; however, participants who received renal denervation treatment experienced a significant decline in both their systolic and diastolic blood pressures, which were lowered by 10.0 mmHg ($p<0.001$) and 5.3 mmHg ($p=0.008$), respectively. This correlation was also reflected when 24-hour ambulatory blood pressure was compared to baseline; the systolic and diastolic blood pressure of patients decreased by 5.5 mmHg ($p=0.04$) and 4.8 mmHg ($p<0.001$), respectively, following renal denervation, whereas there was no significant difference in blood pressure data from participants who underwent the sham procedure.

These statistically significant results were suggested by the authors as being due to both the new procedural approach and the inclusion of uncontrolled hypertensive patients. When summarising the results, co-principal investigator, Prof Michael Boehm, University of Saarland, Homburg/Saar, Germany, commented: "This is particularly important as even small reductions correlate to significant reductions in death, stroke, and overall cardiovascular risk."

Sildenafil Worsens Clinical Scores in Residual Pulmonary Hypertension Patients

SILDENAFIL administration should be avoided when treating valvular heart disease patients with residual pulmonary hypertension, according to the SIOVAC trial presented in a press release from this year's ESC congress, dated 28th August 2017. With valvular disease predicted to become the next cardiac epidemic due to its strong association with age, and the rapidly ageing global population, establishing an effective treatment is essential. Repair or replacement of the dysfunctional valve is the only established treatment; however, symptoms often remain or reappear later.

"Residual pulmonary hypertension is the most important risk factor for death and disability after successful correction of the valvular lesion," commented principal investigator Dr Javier Bermejo, Hospital General Universitario Gregorio Marañon, Madrid, Spain. Pulmonary hypertension is caused by increased blood pressure in the pulmonary artery; in patients with long-standing valvular disease, it causes the high pressure in the left side of the heart to be transmitted backwards, which results in thickening of the lung vessels. Valve treatment may not result in a reversal of this process, which leads to persistent pulmonary hypertension.

It was thought that using the potent vasodilator, sildenafil, would help reduce the pulmonary hypertension pressure. Sildenafil, commonly used to treat erectile dysfunction, showed discrepant results in previous trials for pulmonary hypertension but was believed to be well tolerated. During the SIOVAC trial, 200 patients from 17 public hospitals were randomised into two groups, including one group that received 40 mg sildenafil three times daily, and a placebo group. The double-blind study set out to test the potential of sildenafil in improving long-term outcomes of patients with residual pulmonary hypertension after correction of a valvular lesion.

> We found that in patients with residual pulmonary hypertension after successful corrected valvular heart disease, 6-month treatment with sildenafil leads to worse clinical outcomes than placebo.

The 6-month results were unexpected; 33% of the sildenafil group had worse composite clinical scores (composite of all-cause death, hospital admission for heart failure, worsening exercise tolerance, worsening self-assessment score) than at the beginning of the trial, whereas 15% of the placebo group had worsened scores (odds ratio for improvement: 0.39; 95% confidence interval: 0.22–0.67; $p<0.001$). Sildenafil patients also experienced more hospital admissions, with the overall risk of requiring hospital treatment double for the sildenafil group. Three sildenafil and two placebo patients died during the trial ($p=0.63$). Dr Bermejo commented: "We found that in patients with residual pulmonary hypertension after successful corrected valvular heart disease, 6-month treatment with sildenafil leads to worse clinical outcomes than placebo." He concluded: "Long-term usage of sildenafil for treating residual pulmonary hypertension in patients with valvular heart disease should be avoided."

PRECISION Findings Supported by PRECISION-ABPM Trial Results

ADVERSE cardiovascular events, including increased blood pressure, have long been linked with the use of non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen; however, until recently, data were lacking on the impact from specific drugs. In a late-breaking results presentation at this year's ESC congress, the results from the PRECISION-ABPM trial showed that ibuprofen was associated with an increase in blood pressure and hypertension in osteoarthritis or rheumatoid arthritis patients when compared with celecoxib.

As reported in a ESC press release dated 28th August 2017, investigators enrolled 444 patients from 60 sites across the USA who had either osteoarthritis (n=408, 92%) or rheumatoid arthritis (n=36, 8%) and were either at an increased risk of, or diagnosed with, coronary artery disease. An alteration from baseline in 24-hour ambulatory blood pressure at 4-month follow-up was the primary endpoint of the prospective, double-blind, randomised, non-inferiority trial, designed to determine the effects of selective cyclooxygenase-2 inhibitor celecoxib in comparison with the non-selective NSAIDs, naproxen and ibuprofen.

> ...clinicians need to weigh the potential hazards of worsening blood pressure control when considering the use of these agents.

Patients were randomised 1:1:1 to receive celecoxib (100–200 mg twice daily), ibuprofen (600–800 mg three times daily), or naproxen (375–500 mg twice daily) with matching placebos. Results showed that both ibuprofen and naproxen increased average systolic blood pressure by 3.7 mmHg and 1.6 mmHg, respectively, when measured over 24 hours, whereas celecoxib decreased this

measurement by 0.3 mmHg. Investigators reported a significant difference between celecoxib and ibuprofen at -3.9 mmHg (p=0.009). In addition, the team looked at how many patients developed hypertension when they previously had normal baseline blood pressure, equating to 23.2%, 19.0%, and 10.3% for ibuprofen, naproxen, and celecoxib, respectively (odds ratio: 0.39; p=0.004 for celecoxib; odds ratio: 0.49; p=0.03 for ibuprofen and naproxen).

Principal investigator Prof Frank Ruschitzka, Department of Cardiology, University Hospital, Zürich, Switzerland, commented: "PRECISION-ABPM clearly demonstrates that NSAIDs, particularly ibuprofen, may be not as safe as previously thought. Patients with osteoarthritis and arthritis should continue to consult their doctor before taking NSAIDs or coxibs and clinicians need to weigh the potential hazards of worsening blood pressure control when considering the use of these agents. Since decreasing systolic blood pressure by just 2 mmHg lowers stroke mortality by 10% and ischaemic heart disease mortality by 7%, increases in systolic blood pressure associated with NSAIDs as observed in PRECISION-ABPM should be considered clinically relevant."

Protection of the Brain in Open Heart Surgery

A SIGNIFICANT reduction in the risk of brain infarctions and stroke after heart surgery can be achieved by closing the left atrial appendage, according to the results of the LAACS study, which were presented in a ESC press release, dated 28th August 2017. It is well-known amongst cardiologists that atrial fibrillation is a common occurrence following heart surgery and that this leads to an increased risk of stroke. This is a particular issue as patients may be asymptomatic, meaning they do not undergo prophylactic oral anticoagulation treatment and therefore remain at risk of blood clotting. The lead study author, Dr Jesper Park-Hansen, Department of Cardiology, Bispebjerg/Frederiksberg University Hospital, Copenhagen, Denmark, explained why it was crucial to protect the brain, announcing: "A stroke following open heart surgery can have devastating consequences for patients and their families."

> "Based on the LAACS study, it would be advisable to systematically add surgical closure of the left atrial appendage to planned open heart surgery."

As blood clots tend to develop in the left atrial appendage, it is common practice amongst some heart surgeons to protect against stroke by closing the left atrial appendage. However, this was the first study to date to provide evidence showing that closure of the left atrial appendage during open heart surgery resulted in a reduced risk of brain infarctions and stroke.

One hundred and eighty-seven patients referred for open heart surgery (coronary artery bypass grafting, valve surgery, or both) were enrolled in the study and randomised to either surgical closure of the left atrial appendage (n=101) or no closure (n=86). The study's combined primary endpoint was the incidence of transient ischaemic attack/stroke or silent cerebral infarction. This endpoint was measured at clinical follow-up or detected by magnetic resonance imaging (MRI). As well as shortly before surgery, patients also underwent MRI shortly after discharge and at ≥6-month follow-up. It was found that 16.3% of patients in the control group met the primary endpoint, compared with 5% in the left atrial appendage closure group (hazard ratio: 0.3; 95% confidence interval: 0.1–0.8; p=0.0197). Dr Park-Hansen concluded: "Based on the LAACS study, it would be advisable to systematically add surgical closure of the left atrial appendage to planned open heart surgery. Our results need to be replicated in larger cohorts that can also confirm the safety of the procedure."

Blood Pressure Control Essential in Atrial Fibrillation Patients

VARIABILITY in blood pressure can result in a major risk of adverse effects for all types of atrial fibrillation (AF) patients. Reported in a ESC press release dated 28th August 2017, analysis of a trial comparing AF treatment strategies has revealed the importance of controlling systolic blood pressure in order to reduce major bleeding and the chances of stroke in these vulnerable patients.

More specifically, researchers conducted a post-hoc analysis of the AFFIRM trial. By studying recordings of visit-to-visit variability in mean systolic blood pressure, 3,843 patients were categorised into four quartiles depending on their mean standard deviation in systolic blood pressure, which were defined as: <10.09 mmHg, 10.09–13.85 mmHg, 13.86–17.33 mmHg, and ≥17.34 mmHg for quartiles 1–4, respectively.

The team reported 149 strokes and 248 major bleeding incidences after a mean of 3.6 years of follow-up and concluded that a large range of blood pressure variability directly correlated with higher rates of these events. For example, patients in quartiles 1–4 experienced stroke rates of 2.5%, 3.0%, 3.8%, and 6.2%, respectively (p<0.001). In addition, there was a progressive increase in major bleeding rate across the quartiles, from 10.8% to 11.2%, 15.6%, then 20.8%, respectively (p<0.001). The analysis elucidated that patients in the 3rd and 4th quartiles experienced a significant increase in the risk of both stroke (hazard ratio: 1.85 and 2.33; p=0.042 and p=0.004, respectively) and major bleeding (hazard ratio: 1.92 and 2.88; p=0.009 and p<0.001, respectively), equating to higher mortality rates in these patients.

> "A better effort in controlling blood pressure in the clinical follow-up is pivotal to obtain a better management of patients with AF and improvement of outcomes."

Commenting on the outcomes of this analysis, Dr Marco Proietti, Institute of Cardiovascular Sciences, University of Birmingham, Birmingham, UK, explained: "A better effort in controlling blood pressure in the clinical follow-up is pivotal to obtain a better management of patients with AF and improvement of outcomes." The study authors concluded that consistency in blood pressure control is essential in all types of AF patients, regardless of factors like age and clotting risk.

NIPPON Follow-Up Results: Shorter Dual Antiplatelet Therapy is Beneficial

A SHORT COURSE dual antiplatelet therapy (DAPT) after drug-eluting stent (DES) insertion was found to be as beneficial as a long course to patients at 3-year follow-up, according to a long-term follow-up of the NIPPON study, presented at this year's ESC congress and reported in a ESC press release dated 28th August 2017.

> "In real-world practice, it is not easy to find the balance between risks and benefits of DAPT duration, and consensus criteria for individualisation therapy have not been established."

The original NIPPON results presented at the 2016 ESC congress showed no significant difference in safety and efficacy endpoints in DES patients who were randomised to either a 6 or 18-month course of DAPT. The 3-year follow-up results focussed on 3,307 patients. There was found to be no significant difference in either efficacy or safety between those treated for 6 months versus 18 months; however, a numerically higher rate of better outcomes in the long-term DAPT group (hazard ratio: 1.53; 95% confidence interval: 0.81–2.87; p=0.17) was observed by researchers, including Prof Masato Nakamura, Division of Cardiovascular Medicine, Toho University Ohashi Medical Center, Tokyo, Japan. These results indicated that there was no benefit to patients in continuing DAPT for >6 months as there was no discernible difference between outcomes for both therapy groups.

To further understand these results, researchers conducted a subgroup analysis to evaluate if any subsets of the study population benefited from longer DAPT. It was found that in patients 70–77 years of age with diabetes or more severe coronary artery disease, the efficacy rate was 0.0% for the long-term therapy as opposed to 18.8% for those on short-term therapy. The patients "represent a high-risk population for ischaemic events who might be good candidates for prolonged DAPT," researchers concluded.

Prof Nakamura commented: "In real-world practice, it is not easy to find the balance between risks and benefits of DAPT duration, and consensus criteria for individualisation therapy have not been established." He continued: "The present findings may provide some assistance, although it is essential to obtain confirmation by further investigation." Although the results are intriguing, as Prof Nakamura stated, further research is much needed to assess whether shortening DAPT would still ensure treatment success, and if not, which subgroups would need alternative treatment lengths.

Pooled Analysis Data on Anti-Aldosterones Revealed

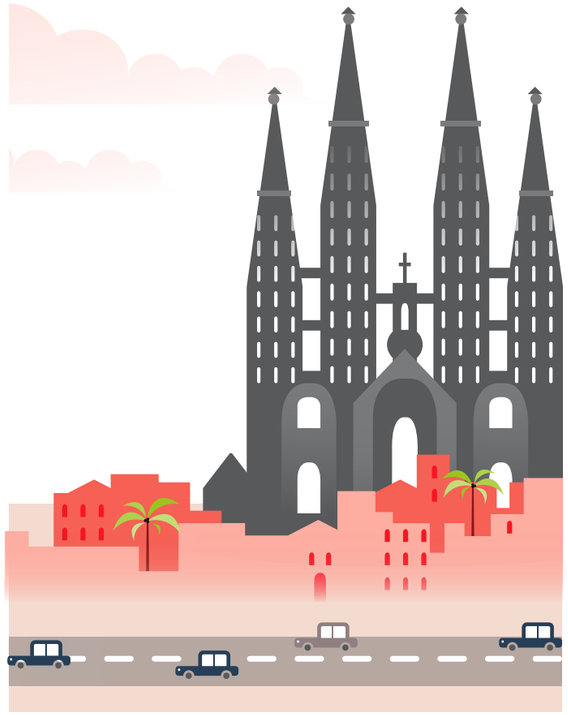
MINERALOCORTICOID receptor antagonists (MRA) could open up a new avenue of treatment for heart patients with ST-segment elevation myocardial infarction (STEMI), according to the results of a pooled data analysis reported in a ESC press release dated 28th August 2017. Investigators used data from the ALBATROSS and REMINDER trials to demonstrate improved outcomes in this patient cohort when MRA are administered alongside traditional treatment methods.

> "These findings highlight the need for more studies that are adequately sized and specifically designed to confirm the potentially major clinical benefit associated with these low-cost treatments."

The trials in question examined the effect of MRA in different cohorts: ALBATROSS considered spironolactone-based MRA in comparison with standard therapy in the treatment of mixed STEMI and non-STEMI patients but did not draw any statistically significant conclusions, while REMINDER exclusively enrolled STEMI patients and demonstrated that administering eplerenone within the first 24 hours of standard therapy reduced a clinico-biological endpoint compared with standard therapy.

Commenting on the motivation for re-examining the results of these previously published trials, Prof Farzin Beygui, Centre Hospitalier Universitaire de Caen, Caen, France, explained: "There was a suggested potential significant mortality reduction in the STEMI subgroup [of the ALBATROSS trial], that was worth investigating further." The analysis included data on a total of 2,241 patients who were randomised to receive either standard therapy with the addition of a MRA (n=1,118) or standard therapy alone (n=1,123). The results were very positive. At a median follow-up of 190 days, there had been significantly fewer deaths in the MRA-treated patient subgroup than those receiving standard therapy alone (0.4% versus 1.6%; stratified odds ratio: 0.22; 95% confidence interval: 0.07–0.65; p=0.006). This demonstrates that STEMI patients who suffer a heart attack are significantly more likely to survive if treated with this regimen than with standard therapy alone.

"The evidence from our analysis is not as strong as from a specifically designed randomised trial; however, the reduction of mortality in STEMI supports the use of MRA in this indication," Prof Beygui commented, adding: "These findings highlight the need for more studies that are adequately sized and specifically designed to confirm the potentially major clinical benefit associated with these low-cost treatments."



A Rethink of Dietary Guidelines?

A RETHINK of dietary guidelines should be undertaken, according to the results of the PURE study, which were reported on in ESC press releases dated 29th August 2017. This study used food frequency questionnaires to assess diet in 135,335 people from 18 low, middle, and high-income countries. All participants were aged 35–70 years.

One aspect of the study focussed on the association between fruit, legume, and vegetable intake with cardiovascular disease risk and death. The researchers noted that current guidelines in the USA and Europe suggest a daily intake of 400–800 g per day of these foods, which can be unaffordable for those with a low income. One of the study investigators, Dr Andrew Mente, Population Health Research Institute, McMaster University, Hamilton, Canada, commented: "Our findings indicate that optimal health benefits can be achieved with a more modest level of consumption, an approach that is likely to be much more affordable." Specific findings included that 375–500 g (equivalent to 3–4 portions) daily of fruits, vegetables, and legumes, was just as beneficial in regard to total mortality as higher servings (hazard ratio [HR]: 0.78; 95% confidence interval [CI]: 0.69–0.88).

The PURE study analysis also considered carbohydrate and fat intake. This analysis was also of great interest, with one of the study investigators, Dr Mahshid Dehghan, Population Health Research Institute, McMaster University, explaining: "Our findings do not support the current recommendation to limit total fat intake to <30% of energy and saturated fat intake to <10% of energy." In the study population, over a median follow-up of 7.4 years, there were 5,796 deaths and 4,784 major cardiovascular events. In this subgroup, it was shown the highest quintile of carbohydrate consumption as compared to the lowest quintile was associated with a 28% increase in the risk of total mortality (HR: 1.28; 95% CI: 1.12–1.46; p≤0.0001) but not cardiovascular disease risk. By comparison, the highest quartile of fat consumption was associated with a 23% reduction of total mortality risk, a 30% decrease in the risk of non-cardiovascular disease mortality, and an 18% reduced risk of stroke. Dr Dehghan suggested that those with a carbohydrate intake of >60% of energy could potentially benefit from reducing their carbohydrate intake and increasing their total fat intake.

The PURE study has offered a wealth of data from a diverse selection of societies, providing an excellent opportunity to discern the impact of diet across heterogenous settings. Further results from the study are awaited with interest.

Praise Given to ESC Guidelines on Hypertrophic Cardiomyopathy

A LARGE cross-continental study has supported following ESC recommendations for the prediction and subsequent prevention of sudden cardiac death (SCD) in hypertrophic cardiomyopathy patients, as described in a ESC press release dated 29th August 2017. Following this study, the 2014 ESC guidelines, which suggest clinicians use the HCM Risk-SCD calculator to estimate patients' 5-year risk of SCD and refer only high-risk patients to receive implantable cardioverter defibrillators (ICD), have demonstrated applicability across the world.

> "We calculated that for every 13 high-risk patients who receive an ICD as recommended by ESC guidelines, 1 patient could potentially be saved from SCD."

Designed using European hypertrophic cardiomyopathy patients only, researchers aimed to validate the application of the HCM Risk-SCD tool across a broader range of healthcare systems and medical expertise, as well as possibly different disease patterns. The HCM-EVIDENCE study evaluated 5-year SCD rates of 3,703 patients from North America, Europe, the Middle East, and Asia in order to test the accuracy of their HCM Risk-SCD scores. Study investigators reported that the scores given by the tool successfully correlated with the actual SCD rates of the patients, and the HCM Risk-SCD calculator was able to accurately differentiate between patients with low and high risks of SCD. More specifically, when the prediction tool classified patients as low-risk by having a SCD incidence of <4% at 5 years, the actual data showed the incidence in these patients as 1.4%. Similarly, high-risk patients had a 5-year incidence of SCD of 8.9%, agreeing with the prediction of >6% incidence using the HCM Risk-SCD calculator.

Dr Constantinos O'Mahony, St. Bartholomew's Centre for Inherited Cardiovascular Disease, St Bartholomew's Hospital and the Centre for Heart Muscle Disease, Institute of Cardiovascular Science, University College London, London, UK, emphasised: "We calculated that for every 13 high-risk patients who receive an ICD as recommended by ESC guidelines, 1 patient could potentially be saved from SCD." Investigators also concluded that by following ESC guidelines and using the HCM Risk-SCD tool, unnecessary ICD implantation in low-risk patients could be avoided. Although all cases of SCD cannot be predicted, Dr O'Mahony noted: "Quantification of risk enhances the shared decision-making process."

New SPRINT Results: Redefining the Ideal Blood Pressure Target

A POST-HOC analysis of previous SPRINT results suggests that for patients with a systolic blood pressure (SBP) of ≥160 mmHg, reducing the severity of blood pressure control may be more beneficial than trying to reach a universal blood pressure target of 120 mmHg, according to a ESC press release dated 28th August 2017. One of the study's authors, Dr Tzung-Dau Wang, National Taiwan University Hospital, Taopei, Taiwan, commented: "A universal blood pressure target may not be appropriate for all, and that for some [...] the harms of aggressive treatment might outweigh the benefits."

The original SPRINT results led to much debate regarding blood pressure guidelines. A total of 9,361 patients with a SBP of ≥130 mmHg were randomly selected for intensive treatment, targeting a SBP of ≤120 mmHg, or standard treatment, with a target of <140 mmHg. Despite better overall outcomes being found in the intensive group, it was suggested that aggressively lowering blood pressure could cause risks to the patient as well as benefits to them.

Therefore, the new SPRINT post-hoc analysis evaluated the results of the 480 patients who originally had a SBP of ≥160 mmHg. Within the group, after adjustment for age and sex, those who received the aggressive treatment had almost three-times the risk of death from any cause compared to those treated less aggressively (4.9% versus 1.7%; hazard ratio: 3.12; 95% confidence interval: 1.00–9.69; p=0.012). By comparison there was no significant difference in increased risk in the intensively treated patients with a lower initial baseline SBP.

Dr Wang commented that these results may inform the original debate sparked by SPRINT. "It seems there was an intricate interaction between each individual's baseline blood pressure, their inherent cardiovascular risk, and their degree of blood pressure reduction, so we have to consider all three of these elements in managing hypertensive patients," he concluded.

> "A universal blood pressure target may not be appropriate for all, and that for some [...] the harms of aggressive treatment might outweigh the benefits."